

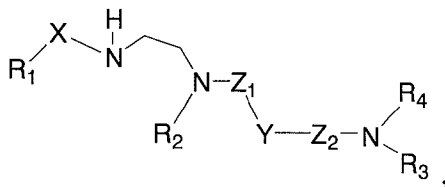
Amendments to the claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of claims:

1-28. (Cancelled)

29. (Original) A compound of the formula:



wherein

X is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, or deleted;

Y is aryl, heteroaryl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl, or C_5 - C_8 heterocycloalkenyl;

each of Z_1 and Z_2 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}=\text{CH}-$, $-\text{CH}=\text{N}-$, $-\text{CH}=\text{N}-\text{NR}-$, $-\text{S}-$, $-\text{O}-$, $-\text{NR}-$, $-\text{C}(\text{O})-$, or $-\text{SO}_2-$;

R_1 is H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl; C_5 - C_8 heterocycloalkenyl, aryl, or heteroaryl;

R_2 is $-\text{A}_1-\text{B}_1-\text{D}_1-\text{E}_1$;

R_3 is $-\text{A}_2-\text{B}_2-\text{D}_2-\text{E}_2$, deleted, or, together with R_4 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl; provided that if R_3 is deleted, $-\text{Z}_2-\text{N}-$ is $-\text{CH}=\text{N}-$; and

R_4 is $-\text{A}_3-\text{B}_3-\text{D}_3-\text{E}_3$ or, together with R_3 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl;

in which each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C₄H₈-, -C₅H₁₀-, -CH₂C(O)-, -C(O)CH₂-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, -CH(C(O)NR₂)-, or deleted; each of B₁, B₂, and B₃, independently, is -NR-, -CH₂-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -C(O)-NR-, -C(S)-NR-, -NR-C(O)-, -NR-C(S)-, -CH(OR)-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl.

30. (Original) The compound of claim 29, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, or -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

31. (Original) The compound of claim 30, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl or heteroaryl; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-,

-SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

32. (Original) The compound of claim 31, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

33. (Original) The compound of claim 31, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.

34. (Original) The compound of claim 31, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.

35. (Original) The compound of claim 32, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-; D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-, -CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.

36. (Original) The compound of claim 35, wherein the compound is one of compounds 60-78, 80-84, 86-109, and 111-126.

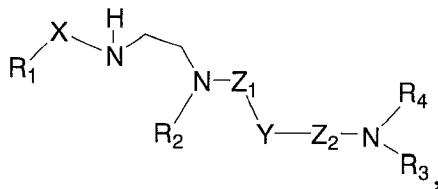
37. (Original) The compound of claim 33, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is -CH(CH₂OH)-; B₁ is -NH-; B₂ is deleted;

B₃ is deleted; D₁ is -CH₂-; D₂ is -CH₂- or deleted; D₃ is -CH₂-; E₁ is heteroaryl; E₂ is H or heteroaryl; and E₃ is aryl.

38. (Original) The compound of claim 37, wherein the compound is compound 79 or 85.

39. (Original) The compound of claim 34, wherein R₁ is heteroaryl; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₃ is deleted; B₁ is -NH-; B₃ is -NH-; D₁ is -CH₂-; D₃ is -C(O)-; E₁ is heteroaryl; and E₃ is heteroaryl.

40. (Original) A compound of the formula:



wherein

X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted;

Y is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, or deleted;

each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-, -CH=N-NR-, -S-, -O-, -NR-, -C(O)-, or -SO₂-;

R₁ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl; C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl;

R₂ is -A₁-B₁-D₁-E₁;

R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl; provided that if R₃ is deleted, -Z₂-N- is -CH=N-; and

R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ cycloalkyl, C₄-C₂₀ cycloalkenyl, C₄-C₂₀ heterocycloalkyl, or C₄-C₂₀ heterocycloalkenyl;

in which each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C₄H₈-, -C₅H₁₀-, -CH₂C(O)-, -C(O)CH₂-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, -CH(C(O)NR₂)-, or deleted; each of B₁, B₂, and B₃, independently, is -NR-, -CH₂-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, -C(O)-NR-, -C(S)-NR-, -NR-C(O)-, -NR-C(S)-, -CH(OR)-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, 5-membered heteroaryl, fused heteroaryl, substituted 6-membered heteroaryl, unsubstituted pyranyl, unsubstituted pyrazinyl, unsubstituted pyrimidinyl, or unsubstituted pyridazinyl; and each of E₂ and E₃, independently, is H, C₁-C₁₀ alkyl, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl.

41. (Original) The compound of claim 40, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, 5-membered heteroaryl, fused heteroaryl,

or substituted 6-membered heteroaryl; and each of E₂ and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

42. (Original) The compound of claim 41, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; E₁ is H, aryl, 5-membered heteroaryl, or fused heteroaryl; and each of E₂ and E₃, independently, is H, aryl, or heteroaryl.

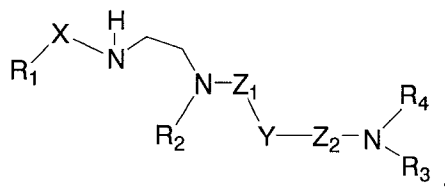
43. (Original) The compound of claim 42, wherein X is -CH₂- or -CH(CH₃)-, Y is deleted, Z₁ is -CH₂-, and Z₂ is -CH₂-.

44. (Original) The compound of claim 43, wherein R₁ is aryl; R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄-; A₂ is deleted; A₃ is deleted; B₁ is -NH-; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl; E₂ is H; and E₃ is aryl.

45. (Original) The compound of claim 43, wherein R₁ is heteroaryl; R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄- or deleted; A₂ is deleted; A₃ is deleted; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl, 5-membered heteroaryl, or fused heteroaryl; E₂ is H; and E₃ is heteroaryl.

46. (Original) The compound of claim 45, wherein the compound is compound 110.

47. (Original) A pharmaceutical composition comprising a compound of the formula:



wherein

X is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, or deleted;

Y is aryl, heteroaryl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl, C_5 - C_8 heterocycloalkenyl, or deleted;

each of Z_1 and Z_2 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}=\text{CH}-$, $-\text{CH}=\text{N}-$, $-\text{CH}=\text{N}-\text{NR}-$, $-\text{S}-$, $-\text{O}-$, $-\text{NR}-$, $-\text{C}(\text{O})-$, or $-\text{SO}_2-$;

R_1 is H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_8 cycloalkyl, C_5 - C_8 cycloalkenyl, C_3 - C_8 heterocycloalkyl; C_5 - C_8 heterocycloalkenyl, aryl, or heteroaryl;

R_2 is $-\text{A}_1-\text{B}_1-\text{D}_1-\text{E}_1$;

R_3 is $-\text{A}_2-\text{B}_2-\text{D}_2-\text{E}_2$, deleted, or, together with R_4 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl; provided that if R_3 is deleted, $-\text{Z}_2-\text{N}-$ is $-\text{CH}=\text{N}-$; and

R_4 is $-\text{A}_3-\text{B}_3-\text{D}_3-\text{E}_3$ or, together with R_3 , is C_4 - C_{20} cycloalkyl, C_4 - C_{20} cycloalkenyl, C_4 - C_{20} heterocycloalkyl, or C_4 - C_{20} heterocycloalkenyl;

in which each of A_1 , A_2 , and A_3 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{C}_4\text{H}_8-$, $-\text{C}_5\text{H}_{10}-$, $-\text{CH}_2\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{CH}_2-$, $-\text{CH}_2\text{SO}_2-$, $-\text{SO}_2\text{CH}_2-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{CH}(\text{CH}_2\text{OR})-$, $-\text{CH}(\text{CH}_2\text{CH}_2\text{OR})-$, $-\text{CH}(\text{COOR})-$, $-\text{CH}(\text{CH}_2\text{COOR})-$, $-\text{CH}(\text{C}(\text{O})\text{NR}_2)-$, or deleted; each of B_1 , B_2 , and B_3 , independently, is $-\text{NR}-$, $-\text{CH}_2-$, or deleted; each of D_1 , D_2 , and D_3 , independently, is $-\text{CH}_2-$, $-\text{C}_2\text{H}_4-$, $-\text{C}_3\text{H}_6-$, $-\text{CH}_2-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{CH}_2-$, $-\text{C}(\text{O})-$, $-\text{SO}_2-$, $-\text{C}(\text{O})-\text{NR}-$, $-\text{C}(\text{S})-\text{NR}-$, $-\text{NR}-\text{C}(\text{O})-$, $-\text{NR}-\text{C}(\text{S})-$, $-\text{CH}(\text{OR})-$, $-\text{CH}(\text{CH}_2\text{OR})-$, $-\text{CH}(\text{CH}_2\text{CH}_2\text{OR})-$, $-\text{CH}(\text{COOR})-$, 1,1-cyclopropylene, or deleted; and each of E_1 , E_2 , and E_3 , independently, is H, C_1 - C_{10} alkyl, C_2 - C_{10} alkenyl, C_2 - C_{10} alkynyl, C_3 - C_8 cycloalkyl,

C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, C₅-C₈ heterocycloalkenyl, aryl, or heteroaryl; each R, independently, being H or C₁-C₁₀ alkyl; and
a pharmaceutically acceptable carrier.

48. (Original) The composition of claim 47, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -SO₂-, or deleted; Y is aryl, heteroaryl, C₅-C₈ cycloalkenyl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, -CH=N-NR-, -NR-, -C(O)-, or -SO₂-; R₁ is C₂-C₁₀ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; R₃ is -A₂-B₂-D₂-E₂, deleted, or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; R₄ is -A₃-B₃-D₃-E₃ or, together with R₃, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH₂-CH=CH-, -CH=CH-CH₂-, or -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, deleted; each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂-CH=CH-, -CH=CH-CH₂-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted; and each of E₁, E₂, and E₃, independently, is H, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl.

49. (Original) The composition of claim 48, wherein X is -CH₂-, -C₂H₄-, -C₃H₆-, -SO₂-, or deleted; Y is aryl, heteroaryl, or deleted; each of Z₁ and Z₂, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH=CH-, or -SO₂-; R₁ is C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; each of A₁, A₂, and A₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -CH₂SO₂-, -SO₂CH₂-, -CH(CH₂OR)-, -CH(CH₂CH₂OR)-, -CH(COOR)-, -CH(CH₂COOR)-, or deleted; each of B₁, B₂, and B₃, independently, is -NH- or deleted; and each of D₁, D₂, and D₃, independently, is -CH₂-, -C₂H₄-, -C₃H₆-, -C(O)-, -SO₂-, -CH(OR)-, -CH(COOR)-, 1,1-cyclopropylene, or deleted.

50. (Original) The composition of claim 49, wherein X is -CH₂- or -CH(CH₃)-, Y is deleted, Z₁ is -CH₂-, and Z₂ is -CH₂-.

51. (Original) The composition of claim 49, wherein X is -CH₂- or -CH(CH₃)-, Y is phenyl, Z₁ is -CH₂- or -SO₂-, and Z₂ is -CH₂- or -SO₂-.

52. (Original) The composition of claim 49, wherein X is -CH₂-, Y is 4,4'-biphenyl, Z₁ is -CH₂-, and Z₂ is -CH₂-.

53. (Original) The composition of claim 49, wherein X is -CH₂-, Y is phenyl, and R₃ is deleted.

54. (Original) The composition of claim 50, wherein R₃ is -A₂-B₂-D₂-E₂; R₄ is -A₃-B₃-D₃-E₃; A₁ is -C₂H₄- or deleted; A₂ is deleted; A₃ is deleted; B₂ is deleted; B₃ is deleted; D₁ is -CH₂-; D₂ is deleted; D₃ is -CH₂-; E₁ is aryl or heteroaryl; E₂ is H; and E₃ is aryl or heteroaryl.

55. (Original) The composition of claim 51, wherein R₃ is -A₂-B₂-D₂-E₂ or, together with R₄, is C₄-C₂₀ heterocycloalkyl or C₄-C₂₀ heterocycloalkenyl; A₁ is -C₂H₄- or -CH(CH₃)CH₂-; A₂ is -C₂H₄- or deleted; A₃ is -CH₂-, -C₂H₄-, -C₃H₆-, -CH(CH₂OH)-, -CH(COOH)-, -CH(CH₂OCH₃)-, -CH(CH₂CH₂OH)-, -CH(CH₂COOH)-, or deleted; B₁ is -NH-, -N(CH₂CH₂OH)-, or -N(CH₂CH₃)-; D₁ is -CH₂-, -CH(CH₃)-, -CH(CH₂OH)-, -CH(CH₂CH₂OH)-, or deleted; D₂ is -CH₂- or deleted; D₃ is -CH₂-, -CH(OH)-, -CH(COOH)-, 1,1-cyclopropylene, or deleted; E₁ is H, C₃-C₈ heterocycloalkyl, aryl, or heteroaryl; E₂ is H, aryl, or heteroaryl; and E₃ is aryl, heteroaryl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, or C₃-C₈ heterocycloalkyl.

56. (Original) The composition of claim 52, wherein R_3 is $-A_2-B_2-D_2-E_2$; R_4 is $-A_3-B_3-D_3-E_3$; A_1 is $-C_2H_4-$; A_2 is deleted; A_3 is $-CH(CH_2OH)-$; B_1 is $-NH-$; B_2 is deleted; B_3 is deleted; D_1 is $-CH_2-$; D_2 is $-CH_2-$ or deleted; D_3 is $-CH_2-$; E_1 is heteroaryl; E_2 is H or heteroaryl; and E_3 is aryl.

57. (Original) The composition of claim 53, wherein R_1 is heteroaryl; R_4 is $-A_3-B_3-D_3-E_3$; A_1 is $-C_2H_4-$; A_3 is deleted; B_1 is $-NH-$; B_3 is $-NH-$; D_1 is $-CH_2-$; D_3 is $-C(O)-$; E_1 is heteroaryl; and E_3 is heteroaryl.